

FIGURE 1

V_{λ}

Leu Glu Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
 5 10 15 20
 Gly Phe Ala Phe Ser Tyr Asp Met Ser Trp Val Arg Gln Ile Pro Glu Lys Arg Leu Glu Trp
 25 30 35 40
 Val Ala Lys Val Ser Ser Gly Gly Gly Ser Thr Tyr Leu Asp Thr Val Gln Gly Arg Phe Thr
 45 50 55 60 65
 Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr Leu Gln Met Ser Ser Leu Asn Ser Glu Asp Thr
 70 75 80 85
 Ala Met Tyr Tyr Cys Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
 90 95 100 105 110
 Thr Val Ser Ala Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
 115 120 125 130

FIGURE 2a

V_{κ}

Glu Leu Val Met Thr Gln Thr Pro Ala Thr Leu Ser Val Thr Pro Gly Asp Ser Val Ser Leu Ser
 5 10 15 20
 Cys Arg Ala Ser Gln Ser Ile Ser Asn His Leu His Trp Tyr Gln Gln Lys Ser His Glu Ser Pro
 25 30 35 40
 Arg Leu Leu Ile Lys Tyr Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly
 45 50 55 60 65
 Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys
 70 75 80 85
 Gln Gln Ser Asn Ser Trp Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
 90 95 100 105

FIGURE 2b

FR 1

V _K	.	.	Thr	Gln	Thr	Pro	Ala	Thr	Leu	Ser	Val	Thr	Pro	Gly	Asp	Ser	Val	Ser	Leu	Ser	Cys
#1	.	.	-	-	Ser	-	Gly	Thr	-	-	Leu	Ser	-	-	Glu	Arg	Ala	Thr	-	-	-
#2	.	.	-	-	Ser	-	Gly	Thr	-	-	Leu	Ser	-	-	Glu	Arg	Gly	Ser	-	-	-
#3	.	.	-	-	Ser	-	Gly	Thr	-	-	Leu	Ser	-	-	Glu	Arg	Ala	Thr	-	-	-
#4	.	.	-	-	Ser	-	Ser	Ser	-	-	Ala	Ser	Val	-	-	Arg	-	Thr	Ile	Thr	-
#5	.	.	-	-	Ser	-	Ser	Ser	-	-	Ala	Ser	Val	-	-	*	-	Thr	Ile	Thr	-
#6	.	.	-	-	Ser	-	Ser	Ser	-	-	Ala	Ser	Val	-	-	Arg	-	Thr	Ile	Thr	-

FIGURE 3a

CDR1

V _K	Arg	Ala	Ser	Gln	Ser	Ile	Ser	Asn	His	Leu	His
#1	-	-	-	-	-	Val	-	Ser	Ser	Tyr	Leu
#2	-	-	-	-	-	Val	-	Ser	Ser	Phe	Leu
#3	-	-	-	-	-	Val	Thr	Ser	Ser	Tyr	Leu
#4	-	-	-	-	-	-	-	Thr	Phe	-	Asn
#5	-	-	-	-	-	-	-	Ser	Tyr	-	Asn
#6	-	-	-	-	-	-	-	Ser	Tyr	-	Asn

FIGURE 3b

FR2

V _K	Trp	Tyr	Gln	Gln	Lys	Ser	His	Glu	Ser	Pro	Arg	Leu	Leu	Ile	Lys
#1	-	-	-	-	-	Pro	Gly	Gln	Ala	-	-	-	-	-	Tyr
#2	-	-	-	-	-	Pro	Gly	Gln	Ala	-	-	-	-	-	Tyr
#3	-	-	-	-	-	Pro	Gly	Gln	Ala	-	-	-	-	-	Tyr
#4	-	-	-	-	-	Pro	Gly	Lys	Ala	-	Lys	Phe	-	-	Tyr
#5	-	-	-	Arg	-	Pro	Gly	Lys	Ala	-	Lys	Leu	-	-	Tyr
#6	-	-	-	-	-	Pro	Gly	Lys	Ala	-	Lys	Leu	-	-	Tyr

FIGURE 3c

CDR2

V _K	Tyr	Ala	Ser	Gln	Ser	Ile	Ser
#1	Gly	-	-	Ser	Arg	Ala	Thr
#2	Gly	-	-	Ser	Arg	Ala	Thr
#3	Gly	-	-	Ser	Arg	Ala	Thr
#4	Ala	-	-	Thr	Leu	Gln	-
#5	Ala	-	-	Thr	Leu	Gln	-
#6	Ala	-	-	Thr	Leu	Gln	-

FIGURE 3d

	LCDR1	LCDR2
mouse	Arg Ala Ser Gln Ser Ile Ser Asn	(Lys) Tyr Ala Ser Gln Ser Ile Ser
selected human		
3 x	Arg Ala Ser Gln Asp Ile Gly Thr	(Lys) Tyr Ala Ser Gln Pro Val Phe
2 x	Arg Ala Ser Gln Asp Ile Gly Asn	(Lys) Tyr Ala Ser Gln Pro Val Phe
1 x	Arg Ala Ser Gln Ser Ile Gly Trp	(Lys) Tyr Ala Ser Gln Ser Ile Ser
unselected human		
	Arg Ser Ser Gln Ser Ile Asn Ile	(Tyr) His Ala Ser Lys Arg Ala Ser
	Arg Ala Ser Gln Ser Val Ser Asn Asn	(Tyr) Arg Ala Ser Ser Arg Ala Thr
	Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr	(Tyr) Lys Val Ser Asn Arg Asp Ser
	Thr Ala Ser Gln Ser Leu Val Tyr Thr Asp Gly Asn Thr	(Tyr) Met Val Ser Asn Arg Asp Ser

FIGURE 4

20051201 15:43:00

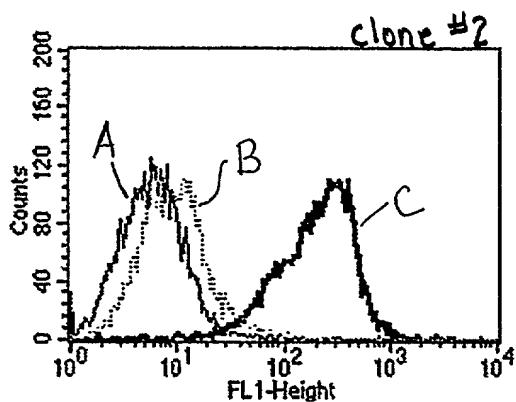


FIGURE 5a

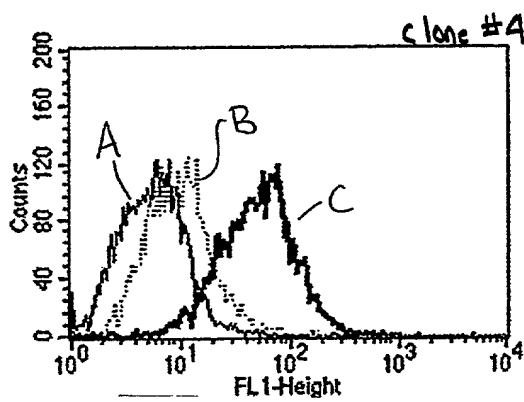


FIGURE 5b

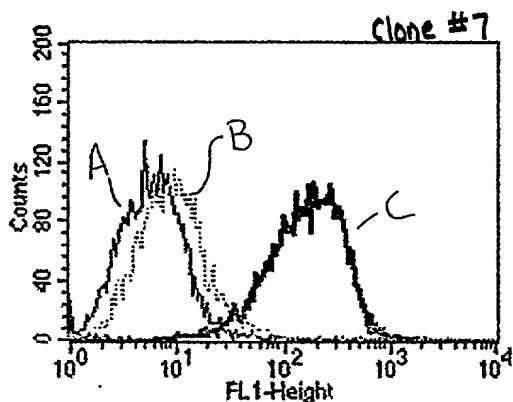


FIGURE 5c

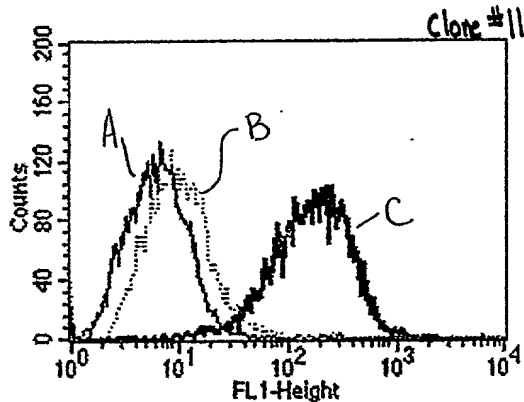


FIGURE 5d

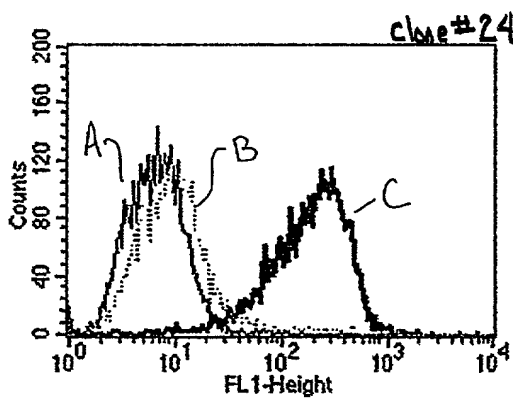


FIGURE 5e

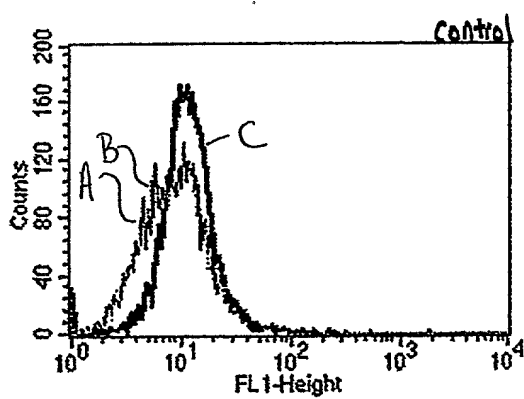


FIGURE 5f

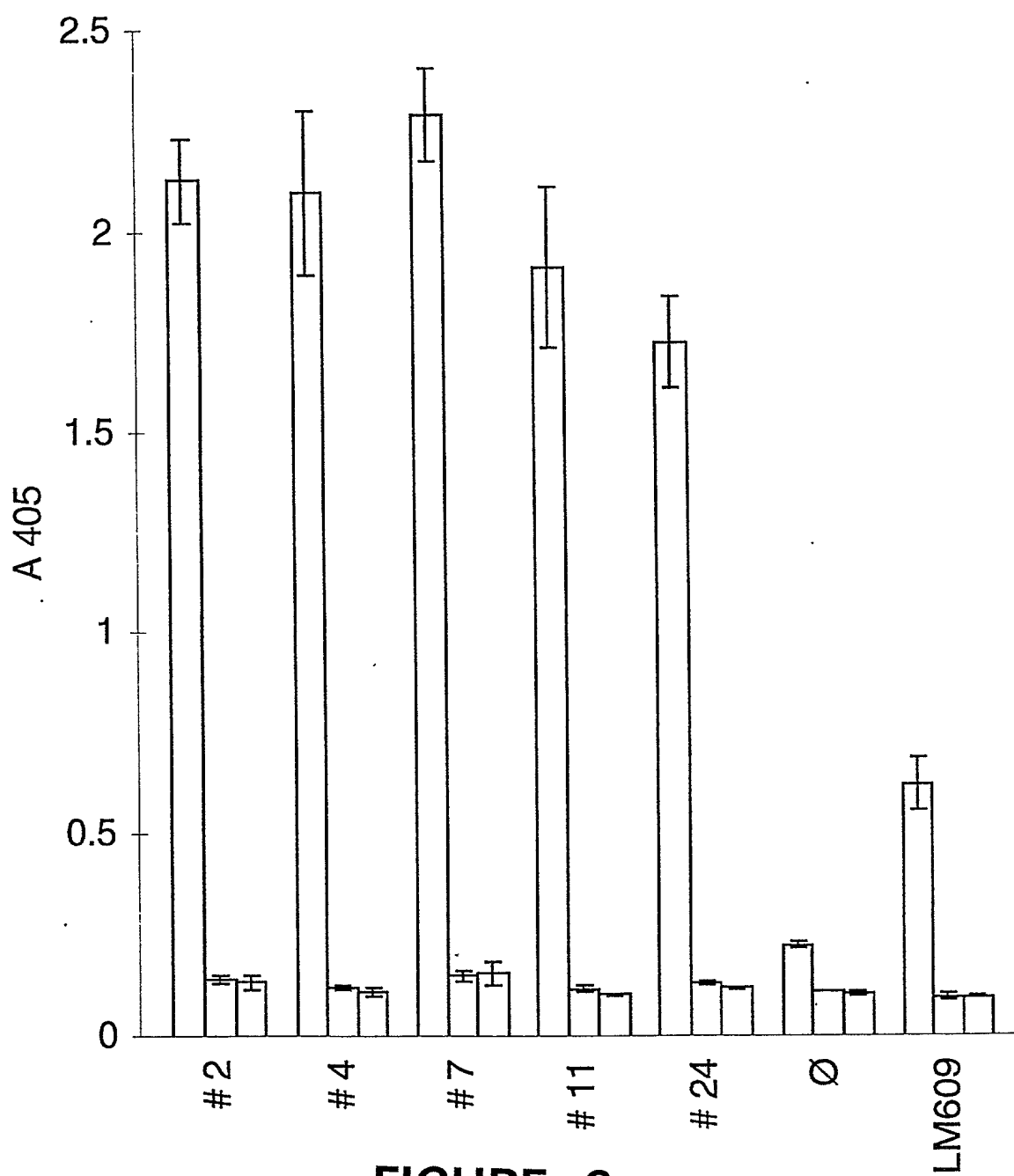


FIGURE 6

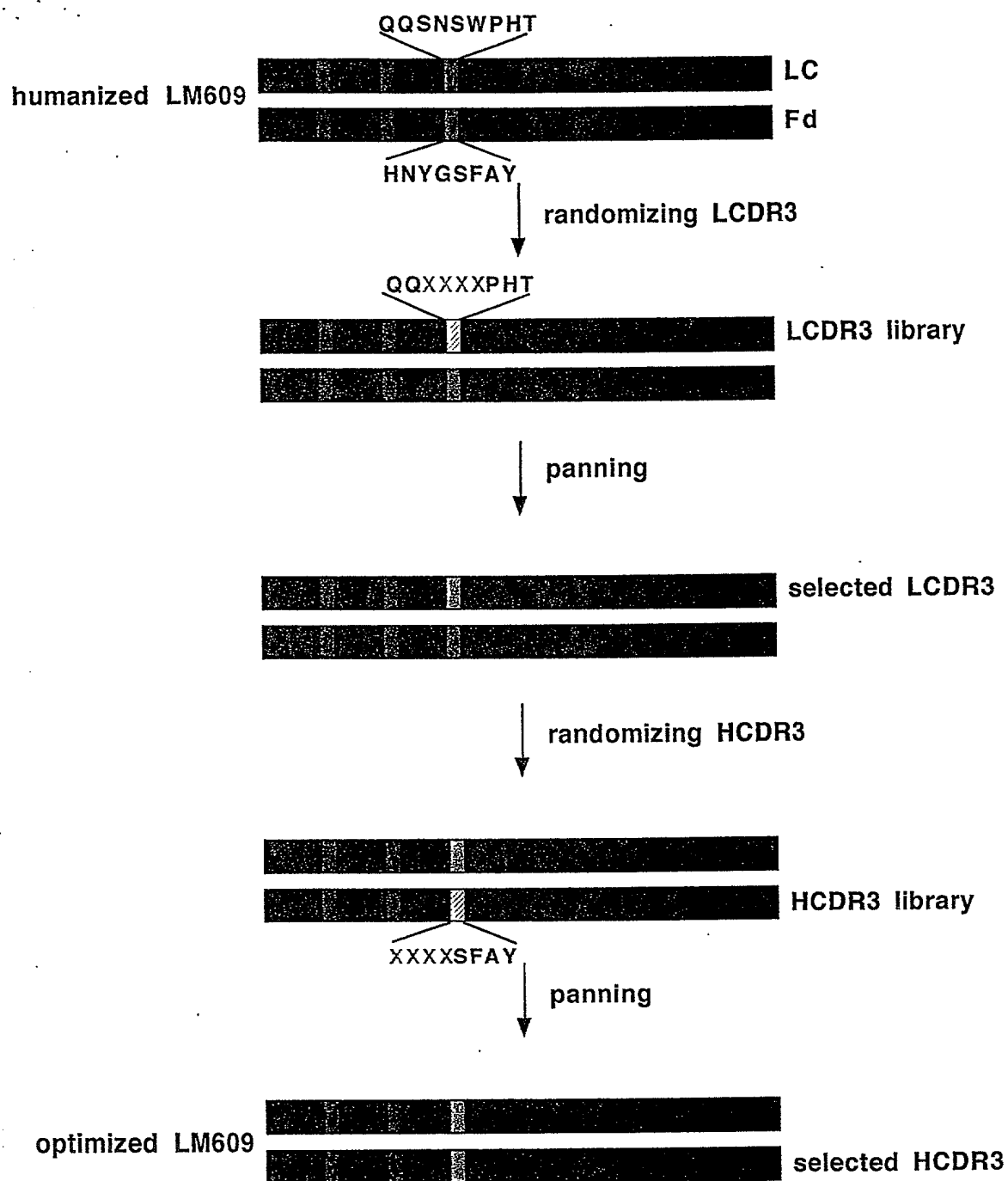


FIGURE 7

FIGURE 8a

V_L amino acid sequences

FR1
mouse
human (Group A)
human (Groups BCDE)

CDR1
mouse
 Arg Ala Ser Gln Ser Ile Ser Asn His Leu His
human (Group A)
 Arg Ala Ser Gln Asp Ile Gly Thr Ser Leu His
human (Groups BCDE)
 Arg Ala Ser Gln Asp Ile Gly Asn Ser Leu His

FR2	<u>mouse</u>	Tyr	Tyr	Gln	Gln	Lys	Ser	His	Glu	Ser	Pro	Arg	Leu	Leu	Ile	Lys
	<u>human (Group A)</u>	Tyr	Tyr	Gln	Gln	Lys	Ser	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Lys
	<u>human (Groups BCDE)</u>	Tyr	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Lys

FIGURE 8b

V_L amino acid sequences

FR3
mouse
Gly Ile Pro ser Arg Phe ser Arg Phe ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Ser Val
Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys
human (Group A)
Gly Val Pro Ser Arg Phe Arg Phe Arg Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Tyr Ser Leu
Glu Ala Glu Asp Phe Ala Val Tyr Tyr Cys
human (Group BCDE)
Gly Val Pro Ser Arg Phe Arg Phe Arg Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu
Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys

[illegible]

FIGURE 8c

V_H amino acid sequences

[illegible]

CDR1	mouse	human	CDR2	mouse	human
Ser Tyr Asp Met	Ser	Trp Val Arg Gln	Ile Pro Glu Lys Arg	Leu Glu Trp	Val Ala
Gly Phe Ala Val	Ser	Trp Val Arg Gln	Ala Pro Gly Gln Arg	Phe Glu Trp	Leu Gly
Arg Gly Tyr	Tyr	Trp Ile Arg Gln	Tyr Pro Gly Lys Gly	Leu Glu Trp	Ile Gly
Gly Gly Tyr	Tyr	Trp Ile Arg His	His Pro Gly Lys Gly	Leu Glu Trp	Ile Gly
Gly Gly Tyr	Tyr	Trp Ile Arg Gln	His Pro Gly Lys Gly	Leu Glu Trp	Ile Gly
Gly Gly Tyr	Tyr	Trp Ile Arg His	His Pro Gly Lys Gly	Leu Glu Trp	Ile Gly
Gly Gly Tyr	Tyr	Trp Ile Arg Gln	His Pro Gly Lys Gly	Leu Glu Trp	Ile Gly
Gly Gly Tyr	Tyr	Trp Ile Arg His	His Pro Gly Lys Gly	Leu Glu Trp	Ile Gly

FIGURE 8d

V_H amino acid sequences

CDR2

mouse
 Lys Val Ser Ser Gly Gly Gly Ser Thr Tyr Tyr Leu Asp Thr Val Gln Gly
human (Group A)
 Gly Ile Val Ala Ser Leu Gly Ser Thr Asp Tyr Ala Gln Lys Phe Gln Asp
human (Group B)
 Tyr Ile His His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
human (Group C)
 Tyr Ile His His Arg Ala Ala Pro Tyr Tyr Asn Pro Ser Leu Lys Ser
human (Group D)
 Tyr Ile His His Ser Ala Gly Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
human (Group E)
 Tyr Ile His His Ser Ala Gly Thr Tyr Tyr Asn Pro Ser Leu Lys Ser

FR3

mouse

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr Leu Gln Met Ser Ser Leu Asn Ser
 Glu Asp Thr Ala Met Thr Val Asp Glu Ser Thr Thr Ala Thr Val Tyr Met Glu Met Arg Asn Leu Arg Ser
human (Group A)
 Lys Leu Thr Ile Thr Val Asp Glu Ser Thr Thr Ala Thr Val Tyr Met Glu Met Arg Asn Leu Arg Ser
 Asp Asp Thr Ala Val Tyr Tyr Cys Ala Ar
human (Group B)
 Arg Val Thr Ile Ala Ile Asp Thr Ser Lys Asn Gln Leu Ser Leu Arg Leu Thr Ser Val Thr Ala
 Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
human (Group C)
 Arg Val Thr Ile Ser Val Asp Thr Ser Arg Asn Asn Gln Ile Ser Leu Lys Leu Arg Ser Val Thr Ala
 Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
human (Group D)
 Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu Lys Leu Thr Ser Val Thr Ala
 Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
human (Group E)
 Arg Val Thr Met Ser Ala Asp Thr Ser Lys Asn Gln Leu Ser Leu Lys Leu Ala Ser Val Thr Ala
 Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg

FIGURE 8e

V_H amino acid sequences

CDR3	mouse	FR4	mouse
His Asn Tyr Gly	Ser Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu Val Thr Val Ser Ala
<u>human (Group A)</u>		<u>human (Group A)</u>	
His Asn Tyr Gly	Ser Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu Val Thr Val Ser Ser
<u>human (Group B)</u>		<u>human (Group B)</u>	
His Asn Tyr Gly	Ser Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu Val Thr Val Ser Ser
<u>human (Group C)</u>		<u>human (Group C)</u>	
His Asn Tyr Gly	Ser Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu Val Thr Val Ser Ser
<u>human (Group D)</u>		<u>human (Group D)</u>	
His Asn Tyr Gly	Ser Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu Val Thr Val Ser Ser
<u>human (Group E)</u>		<u>human (Group E)</u>	
His Asn Tyr Gly	Ser Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu Val Thr Val Ser Ser